

In the Claims

1 (currently amended). A stabilized liquid pharmaceutical composition comprising an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, ~~wherein said formulation is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant.~~

2 (original). The composition according to claim 1, wherein said interferon is IFN-beta.

3 (currently amended). The composition according to ~~claims 1 or 2~~ claim 2, wherein said IFN-beta is recombinant human IFN-beta.

4 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said buffer is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, where the specified pH is about 3 to about 6.

5 (currently amended). The composition according to ~~any of the preceding claim~~ claim 4, wherein said pH is 3.8.

6 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said buffer is present at a concentration of about 5 mM to 500 mM.

7 (currently amended). The composition according to ~~any of the preceding claims~~ claim 6, wherein said buffer is present at a concentration of about 50 mM.

8 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein the buffer is acetate buffer.

9 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said isotonicity agent is mannitol.

10 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said isotonicity agent is present at a concentration of about 0.5 mg/ml to about 500 mg/ml.

11 (currently amended). The composition according to ~~any of the preceding claims~~ claim 10, wherein said isotonicity agent is present at a concentration of about 50 mg/ml.

12 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said the antioxidant is methionine.

13 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said the antioxidant is present at a concentration of about 0.01 to about 5 mg/ml.

14 (currently amended). The composition according to ~~any of the preceding claims~~ claim 13, wherein said the antioxidant is present at a concentration of about 0.1 mg/ml.

15 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said interferon is present at a concentration of about 10 µg/ml to about 800 µg/ml.

16 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said cyclodextrin is present at a molar ratio vs. interferon of from 500-fold molar excess up to 700-fold molar excess.

17 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said interferon is present at a concentration of about 44, 88 or 276 µg/ml.

18 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein said composition is an aqueous solution.

19 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, further comprising a bacteriostatic agent.

20 (currently amended). The composition according to ~~any of the preceding claims~~ claim 19, wherein said bacteriostatic agent is benzyl alcohol.

21 (currently amended). The composition according to ~~any of the preceding claims~~ claim 18, wherein said bacteriostatic agent is present at a concentration of about 0.1% to about 2%.

22 (currently amended). The composition according to ~~any of the preceding claims~~ claim 18, wherein said bacteriostatic agent is present at a concentration of about 0.2 or 0.3%.

23 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein the isotonicity agent is mannitol, the anti-oxidant is methionine and the interferon is interferon beta.

24 (currently amended). The composition according to ~~any of the preceding claims~~ claim 1, wherein the composition is the following liquid formulation:

Interferon beta-1a	44	µg/mL
HPBCD	1.9	mg/mL
Methionine	0.1	mg/mL
Mannitol	50	mg/mL
acetate buffer up to	1	mL

25 (currently amended). A method for preparing a stabilized liquid pharmaceutical composition comprising adding according any of claims 1 to 24, wherein said method comprises adding a calculated amounts of 2-hydroxypropyl-beta-cyclodextrin, antioxidant and isotonicity agent to the buffered solution and then adding the interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof.

26-31 (canceled).

32 (new). An article of manufacture comprising a container containing a stabilized liquid pharmaceutical composition comprising:

- a) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- b) interferon-beta (IFN-beta) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- c) recombinant interferon-beta (IFN-beta) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- d) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a buffer that is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, wherein the specified pH is about 3 to about 6;
- e) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises 2-

hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a buffer that is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, wherein said pH is 3.8;

- f) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said buffer is present at a concentration of about 5 mM to 500 mM;
- g) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said buffer is present at a concentration of about 50 mM;
- h) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises an acetate buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- i) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is mannitol;
- j) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is present at a concentration of about 0.5 mg/ml to about 500 mg/ml;
- k) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is present at a concentration of about 50 mg/ml;

- l) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is methionine;
- m) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is present at a concentration of about 0.01 to about 5 mg/ml;
- n) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is present at a concentration of about about 0.1 mg/ml;
- o) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said interferon is present at a concentration of about 10 µg/ml to about 800 µg/ml;
- p) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said cyclodextrin is present at a molar ratio vs. interferon of from 500-fold molar excess up to 700-fold molar excess;
- q) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said interferon is present at a concentration of about 44, 88 or 276 µg/ml;
- r) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a

buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said composition is an aqueous solution;

- s) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent;
- t) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is benzyl alcohol;
- u) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is present at a concentration of about 0.1% to about 2%;
- v) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is present at a concentration of about 0.2 or 0.3%;
- w) an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein the isotonicity agent is mannitol, the anti-oxidant is methionine and the interferon is interferon beta; or
- x) a composition comprising an interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity

agent and an anti-oxidant, wherein the composition is the following liquid formulation:

Interferon beta-1a	44	µg/mL
HPBCD	1.9	mg/mL
Methionine	0.1	mg/mL
Mannitol	50	mg/mL
acetate buffer up to	1	mL

; and

wherein said container is hermetically sealed in conditions that are sterile and appropriate for storage prior to use.

33 (new). The article of manufacture according to claim 32, wherein said container is for mono-dose or multi-dose administration.

34 (new). The article of manufacture according to claim 33, wherein said container is a pre-filled syringe for mono-dose administration.

35 (new). The article of manufacture according to claim 33, wherein said container is a vial.

36 (new). The article of manufacture according to claim 33, wherein said container is a cartridge for an auto-injector.

37 (new). The article of manufacture according to claim 32, wherein said article of manufacture is a kit for multi-dose administration of a pharmaceutical composition, said kit comprising a first container, said first container comprising a container containing said stabilized liquid pharmaceutical composition and a second container filled with a solution of a bacteriostatic agent.